

(1) GENERAL INFORMATION

(i) APPLICANT: Lin et al.

(ii) TITLE OF INVENTION: Glial Derived Neurotrophic Factor

(iii) NUMBER OF SEQUENCES: 24

(iv) CORRESPONDENCE ADDRESS:

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(C) CITY: Denver
(D) STATE: Colorado
(E) COUNTRY: USA
(F) ZIP: 80237

(v) COMPUTER READABLE FORM:

(A) MEDIUM TYPE: Diskette, 3.5 inch, 1.44 MB storage
(B) COMPUTER: IBM compatible
(C) OPERATING SYSTEM: MS DOS
(D) SOFTWARE: Wordperfect 5.1

(vi) CURRENT APPLICATION DATA:

(A) APPLICATION NUMBER: 08/182,183
(B) FILING DATE: 5-MAY-1994

(vii) PRIOR APPLICATION DATA:

(A) APPLICATION NUMBER: 07/788,423, 07/774,109, 07/764,685
(B) FILING DATE: 06-NOV-1991, 08-OCT-1991, 20-SEP-1991

(viii) ATTORNEY/AGENT INFORMATION:

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(ix) TELECOMMUNICATION INFORMATION:

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(2) INFORMATION FOR SEQ ID NO:1

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 25 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(v) FRAGMENT TYPE: N-terminal fragment

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:1:

Ser Pro Asp Lys Gln Ala Ala Ala Leu Pro Arg Arg Glu Arg Asn Xaa
5 10 15

Gln Ala Ala Ala Ala Ser Pro Asp Asn

(2) INFORMATION FOR SEQ ID NO:2

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 13 amino acids
- (B) TYPE: amino acid
- (C) TOPOLOGY: linear

(v) FRAGMENT TYPE: internal fragment

(ix) FEATURE: Xaa is either Lys or Gln

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:2:

Asp Xaa Ile Leu Lys Asn Leu Gly Arg Val Arg Arg Leu

(2) INFORMATION FOR SEQ ID NO:3

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 900 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ix) FEATURE:

- (A) NAME/KEY: nucleic acid for rat GDNF

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:3:

CCCCCGGGCT GCAGGAATTC GGGG GTC TAC GGA GAC CGG ATC CGA GGT GCC GCC	54
Val Tyr Gly Asp Arg Ile Arg Gly Ala Ala	
-90	-85
GCC GGA CGG GAC TCT AAG ATG AAG TTA TGG GAT GTC GTG GCT GTC TGC	102
Ala Gly Arg Asp Ser Lys Met Lys Leu Trp Asp Val Val Ala Val Cys	
-80	-75
-70	
CTG GTG TTG CTG CAC ACC GCG TCT GCC TTC CCG CTG CCC GCC GGT AAG	150
Leu Val Leu Leu His Thr Ala Ser Ala Phe Pro Leu Pro Ala Gly Lys	
-65	-60
-55	
AGG CTT CTC GAA GCG CCC GCC GAA GAC CAC TCC CTC GGC CAC CGC CGC	198
Arg Leu Leu Glu Ala Pro Ala Glu Asp His Ser Leu Gly His Arg Arg	
-50	-45
-40	
GTG CCC TTC GCG CTG ACC AGT GAC TCC AAT ATG CCC GAA GAT TAT CCT	246
Val Pro Phe Ala Leu Thr Ser Asp Ser Asn Met Pro Glu Asp Tyr Pro	
-35	-30
-25	-20
GAC CAG TTT GAT GAC GTC ATG GAT TTT ATT CAA GCC ACC ATC AAA AGA	296
Asp Gln Phe Asp Asp Val Met Asp Phe Ile Gln Ala Thr Ile Lys Arg	
-15	-10
-5	

CTG AAA AGG TCA CCA GAT AAA CAA GCG GCG GCA CTT CCT CGA AGA GAG Leu Lys Arg Ser Pro Asp Lys Gln Ala Ala Ala Leu Pro Arg Arg Glu	342
1 5 10	
AGG AAC CGG CAA GCT GCA GCT GCC AGC CCA GAG AAT TCC AGA GGG AAA Arg Asn Arg Gln Ala Ala Ala Ser Pro Glu Asn Ser Arg Gly Lys	390
15 20 25	
GGT CGC AGA GGC CAG AGG GGC AAA AAT CGG GGG TGC GTC TTA ACT GCA Gly Arg Arg Gly Gln Arg Gly Lys Asn Arg Gly Cys Val Leu Thr Ala	438
30 35 40 45	
ATA CAC TTA AAT GTC ACT GAC TTG GGT TTG GGC TAC GAA ACC AAG GAG Ile His Leu Asn Val Thr Asp Leu Gly Leu Gly Tyr Glu Thr Lys Glu	486
50 55 60	
GAA CTG ATC TTT CGA TAT TGT AGC GGT TCC TGT GAA GCG GCC GAG ACA Glu Leu Ile Phe Arg Tyr Cys Ser Gly Ser Cys Glu Ala Ala Glu Thr	534
65 70 75	
ATG TAC GAC AAA ATACTA AAA AAT CTG TCT CGA AGT AGA AGG CTA ACA Met Tyr Asp Lys Ile Leu Lys Asn Leu Ser Arg Ser Arg Arg Leu Thr	582
80 85 90	
AGT GAC AAG GTA GGC CAG GCA TGT TGC AGG CCG GTC GCC TTC GAC GAC Ser Asp Lys Val Gly Gln Ala Cys Cys Arg Pro Val Ala Phe Asp Asp	630
95 100 105	
GAC CTG TCG TTT TTA GAC GAC AGC CTG GTT TAC CAT ATC CTA AGA AAG Asp Leu Ser Phe Leu Asp Asp Ser Leu Val Tyr His Ile Leu Arg Lys	678
110 115 120 125	
CAT TCC GCT AAA CGG TGT GGA TGT ATC TGA CCCTGGCTCC AGAGACTGCT His Ser Ala Lys Arg Cys Gly Cys Ile	728
130	
GTGTATTGCA TTCCCTGCTAC ACTGCGAAGA AAGGGACCAA GGTTCCCAGG AAATATTTGC	788
CCAGAAAGGA AGATAAGGAC CAAGAAGGCA GAGGCAGAGG CGGAAGAAGA AGAAGAAAAG	848
AAGGACGAAG GCAGCCATCT GTGGGAGCCT GTAGAAGGGAG GCCCAGCTAC AG	900

(2) INFORMATION FOR SEQ ID NO:4

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 134 amino acid residues
- (B) TYPE: amino acid
- (D) TOPOLOGY: linear

(ix) FEATURE:

- (A) NAME/KEY: inferred amino acid sequence for mature rat GDNF

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:4:

Ser Pro Asp Lys Gln Ala Ala Ala Leu Pro Arg Arg Glu Arg Asn Arg
 1 5 10 15
 Gln Ala Ala Ala Ala Ser Pro Glu Asn Ser Arg Gly Lys Gly Arg Arg
 20 25 30
 Gly Gln Arg Gly Lys Asn Arg Gly Cys Val Leu Thr Ala Ile His Leu
 35 40 45
 Asn Val Thr Asp Leu Gly Leu Gly Tyr Glu Thr Lys Glu Glu Leu Ile
 50 55 60
 Phe Arg Tyr Cys Ser Gly Ser Cys Glu Ala Ala Glu Thr Met Tyr Asp
 65 70 75 80
 Lys Ile Leu Lys Asn Leu Ser Arg Ser Arg Arg Leu Thr Ser Asp Lys
 85 90 95
 Val Gly Gln Ala Cys Cys Arg Pro Val Ala Phe Asp Asp Asp Leu Ser
 100 105 110
 Phe Leu Asp Asp Ser Leu Val Tyr His Ile Leu Arg Lys His Ser Ala
 115 120 125
 Lys Arg Cys Gly Cys Ile
 130

(2) INFORMATION FOR SEQ ID NO:5

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 562 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ix) FEATURE:

- (A) NAME/KEY: nucleic acid sequence for human GDNF

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:5:

ATTTTCTCTT TTCTTTTGA ACAGCA AAT ATG CCA GAG GAT TAT CCT GAT CAG 53
 Asn Met Pro Glu Asp Tyr Pro Asp Gln
 TTC GAT GAT GTC ATG GAT TTT ATT CAA GCC ACC ATT AAA AGA CTG AAA 101
 Phe Asp Asp Val Met Asp Phe Ile Gln Ala Thr Ile Lys Arg Leu Lys
 AGG TCA CCA GAT AAA CAA ATG GCA GTG CTT CCT AGA AGA GAG CGG AAT 149
 Arg Ser Pro Asp Lys Gln Met Ala Val Leu Pro Arg Arg Glu Arg Asn
 1 5 10 15
 CGG CAG GCT GCA GCT GCC AAC CCA GAG AAT TCC AGA GGA AAA GGT CGG 197
 Arg Gln Ala Ala Ala Asn Pro Glu Asn Ser Arg Gly Lys Gly Arg
 20 25 30

AGA GGC CAG AGG GGC AAA AAC CGG GGT TGT GTC TTA ACT GCA ATA CAT Arg Gly Gln Arg Gly Lys Asn Arg Gly Cys Val Leu Thr Ala Ile His 35 40 45	245
TTA AAT GTC ACT GAC TTG GGT CTG GGC TAT GAA ACC AAG GAG GAA CTG Leu Asn Val Thr Asp Leu Gly Leu Gly Tyr Glu Thr Lys Glu Glu Leu 50 55 60	293
ATT TTT AGG TAC TGC AGC GGC TCT TGC GAT GCA GCT GAG ACA ACG TAC Ile Phe Arg Tyr Cys Ser Gly Ser Cys Asp Ala Ala Glu Thr Thr Tyr 65 70 75	341
GAC AAA ATA TTG AAA AAC TTA TCC AGA AAT AGA AGG CTG GTG ACT GAC Asp Lys Ile Leu Lys Asn Leu Ser Arg Asn Arg Arg Leu Val Ser Asp 80 85 90 95	389
AAA GTA GGG CAG GCA TGT TGC AGA CCC ATC GCC TTT GAT GAT GAC CTG Lys Val Gly Gln Ala Cys Cys Arg Pro Ile Ala Phe Asp Asp Asp Leu 100 105 110	437
TCG TTT TTA GAT GAT AAC CTG GTT TAC CAT ATT CTA AGA AAG CAT TCC Ser Phe Leu Asp Asp Asn Leu Val Tyr His Ile Leu Arg Lys His Ser 115 115 120 120 125 125	485
GCT AAA AGG TGT GGA TGT ATC TGA CTCCGGCTCC AGAGACTGCT GTGTATTGCA Ala Lys Arg Cys Gly Cys Ile 130 130	539
TTCCCTGCTAC AGTGCAAAGA AAG	562

(2) INFORMATION FOR SEQ ID NO:6

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 134 amino acid residues
- (B) TYPE: amino acid
- (D) TOPOLOGY: linear

(ix) FEATURE:

- (A) NAME/KEY: inferred amino acid sequence for mature human GDNF

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:6:

Ser Pro Asp Lys Gln Met Ala Val Leu Pro Arg Arg Glu Arg Asn Arg 1 5 10 15
Gln Ala Ala Ala Ala Asn Pro Glu Asn Ser Arg Gly Lys Gly Arg Arg 20 25 30
Gly Gln Arg Gly Lys Asn Arg Gly Cys Val Leu Thr Ala Ile His Leu 35 40 45
Asn Val Thr Asp Leu Gly Leu Gly Tyr Glu Thr Lys Glu Glu Leu Ile 50 55 60

Phe Arg Tyr Cys Ser Gly Ser Cys Asp Ala Ala Glu Thr Thr Tyr Asp
65 70 75 80

Lys Ile Leu Lys Asn Leu Ser Arg Asn Arg Arg Leu Val Ser Asp Lys
85 90 95

Val Gly Gln Ala Cys Cys Arg Pro Ile Ala Phe Asp Asp Asp Leu Ser
100 105 110

Phe Leu Asp Asp Asn Leu Val Tyr His Ile Leu Arg Lys His Ser Ala
115 120 125

Lys Arg Cys Gly Cys Ile
130

(2) INFORMATION FOR SEQ ID NO:7

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 20 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ix) FEATURE:

- (A) NAME/KEY: oligonucleotide probe
- (D) OTHER INFORMATION: N at positions 3, 15, and 18 is inosine

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:7:

CCNGAYAAC ARG CNG CNGC

20

(2) INFORMATION FOR SEQ ID NO:8

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 223 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ix) FEATURE:

- (A) NAME/KEY: nucleic acid sequence for human GDNF

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:8:

TTCTCTCCCC CACCTCCCGC CTGCCCGCGC A GGT GCC GCC GGA CGG GAC TTT
Gly Ala Ala Ala Gly Arg Asp Phe
-5

55

AAG ATG AAG TTA TGG GAT GTC GTG GCT GTC TGC CTG GTG CTG CTC CAC
Lys Met Lys Leu Trp Asp Val Val Ala Val Cys Leu Val Leu Leu His
1 5 10 15

103

ACC GCG TCC GCC TTC CCG CTG CCC GCC GGT AAG AGG CCT CCC GAG GCG
Thr Ala Ser Ala Phe Pro Leu Pro Ala Gly Lys Arg Pro Pro Glu Ala

151

20	25	30	
CCC GCC GAA GAC CGC TCC CTC GGC CGC CGC CGC GCG CCC TTC GCG CTG			199
Pro Ala Glu Asp Arg Ser Leu Gly Arg Arg Ala Pro Phe Ala Leu			
35	40	45	
AGC AGT GAC TGTAAGAACCC GTTCC			223
Ser Ser Asp			
50			

(2) INFORMATION FOR SEQ ID NO:9

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 12 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
- (ix) FEATURE:
 - (A) NAME/KEY: linker

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:9:

CCCGAATTCTGG GG

(2) INFORMATION FOR SEQ ID NO:10

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 7 amino acid residues
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:10:

Pro Asp Lys Gln Ala Ala Ala

(2) INFORMATION FOR SEQ ID NO:11

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 33 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
- (ix) FEATURE:
 - (A) NAME/KEY: nucleic acid sequence from pBluescript SK-76.1

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:11:

GAG AGG AAC CGG CAA GCT GCW GMW GYM WGM CCW

33

(2) INFORMATION FOR SEQ ID NO:12

- (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 11 amino acid residues
- (B) TYPE: amino acid
- (D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:12:

Glu Arg Asn Arg Gln Ala Ala Ala Ala Ser Pro

(2) INFORMATION FOR SEQ ID NO:13

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 20 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear

(ix) FEATURE:

- (A) NAME/KEY: oligonucleotide DHD-26
- (D) OTHER INFORMATION: N at positions 9 and 12 are inosine

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:13:

ARRTTYTTNA RNATYTTTRTC

20

(2) INFORMATION FOR SEQ ID NO:14

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 7 amino acid residues
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:14:

Asp Lys Ile Leu Lys Asn Leu

(2) INFORMATION FOR SEQ ID NO:15

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 17 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear

(ix) FEATURE:

- (A) NAME/KEY: oligonucleotide primer PD1

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:15:

GACGGGACTC TAAGATG

17

(2) INFORMATION FOR SEQ ID NO:16

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 20 base pairs

- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ix) FEATURE:

- (A) NAME/KEY: oligonucleotide primer DHD23
- (D) OTHER INFORMATION: N at positions 3, 6, and 18 is inosine

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:16:

GCNGCNGCYT GYTTTCNGG

20

(2) INFORMATION FOR SEQ ID NO:17

- (i) SEQUENCE CHARACTERISTICS:
- (A) LENGTH: 17 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ix) FEATURE:

- (A) NAME/KEY: oligonucleotide primer LF2

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:17:

CGAGACAATG TACGACA

17

(2) INFORMATION FOR SEQ ID NO:18

- (i) SEQUENCE CHARACTERISTICS:
- (A) LENGTH: 17 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ix) FEATURE:

- (A) NAME/KEY: oligonucleotide primer PD2

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:18:

CTCTGGAGCC AGGGTCA

17

(2) INFORMATION FOR SEQ ID NO:19

- (i) SEQUENCE CHARACTERISTICS:
- (A) LENGTH: 26 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ix) FEATURE:

- (A) NAME/KEY: oligonucleotide primer PD1

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:19:

CCCGAATTCTG ACGGGACTCT AAGATG

26

(2) INFORMATION FOR SEQ ID NO:20

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 24 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ix) FEATURE:

- (A) NAME/KEY: oligonucleotide primer LFA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:20:

CGGTGGCCAG AGGGAGTGGT CTTC

24

(2) INFORMATION FOR SEQ ID NO:21

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 46 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ix) FEATURE:

- (A) NAME/KEY: oligonucleotide primer PD3

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:21:

CGCGGATCCA ATAAGGAGGA AAAAAAAATGT CACCAAGATAA ACAAAAT

46

(2) INFORMATION FOR SEQ ID NO:22

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 26 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ix) FEATURE:

- (A) NAME/KEY: oligonucleotide primer PD4

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:22:

CGCGGTACCC AGTCTCTGGT GCCGGT

26

(2) INFORMATION FOR SEQ ID NO:23

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 33 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(ix) FEATURE:

(A) NAME/KEY: adapter fragment for plasmid pCJ1

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:23:

GATCTAGAAT TGTCAATGTTT GACAGCTTAT CAT

33

(2) INFORMATION FOR SEQ ID NO:24

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 37 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: double
(D) TOPOLOGY: linear

(ix) FEATURE:

(A) NAME/KEY: polylinker sequence for plasmid pCJX1-1

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:24

AATTCCCGGG TACCAAGATCT GAGCTCACTA GTCTGCA

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Date: July 19, 1994
Applicant: Lin et al.
Serial NO. 08/182,183
For: Glial Derived Neurotrophic FActor

RECEIPT IS HEREBY ACKNOWLEDGED OF Reply to Notice to File Missing Parts; Statement Under 37 CFR 1.821(f) and 3 1/2 inch floppy disc; and Statement Under 37 CFR Section 1.125.



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